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Kathy Meuse
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Thomas L. Benjamin et al.	Art Unit:	1632
Serial No.:	09/812,633	Examiner:	Q. Janice Li
Filed:	March 19, 2001	Customer No.:	21559
Title:	DIAGNOSING AND TREATING CANCER CELLS USING SAL2		

Commissioner for Patents
Washington, D.C. 20231

DECLARATION UNDER 37 C.F.R. § 1.132 OF DR. THOMAS BENJAMIN, PhD

I declare:

1. I am an inventor of the subject matter that is described and claimed in the above-captioned patent application.

2. I have read the Office Action mailed on August 14, 2002 in connection with the above-referenced patent application.

3. We have found multiple polymorphisms in the SAL2 [illegible] using techniques known in the art at the time the application was filed. For example, we have described

in the specification a polymorphism (on pages 36 and 37) at amino acid position 73 of the $p150^{Sal2}$ protein, characterized by the substitution of a serine residue with a proline residue. Referring to Figure 11, we have found loss of heterozygosity (LOH) at this site, or loss of the 73S allele, in an ovarian tumor relative to healthy tissue. Page 36 (line 28) of the specification also discloses of a G744R substitution in ovarian carcinoma cell lines, which we have also found in human ovarian tumor samples. In addition to the S73C and the G744R polymorphisms in the $p150^{Sal2}$ gene described throughout the specification (e.g., at pages 36 and 37), multiple polymorphisms associated with proliferative diseases have been found elsewhere in the $p150^{Sal2}$ gene (summarized in Exhibit 1). Tumor samples and matching healthy tissues isolated from heterozygous individuals were analyzed for LOH at such polymorphic positions. In particular, LOH at amino acid position 120 (S120P) was only observed in tumor samples (P/P) while healthy tissues were heterozygous (S/P). Based on our analysis of ovary tumor and normal tissue screened to date, we have found that LOH only occurs in tumor samples.

4. Exhibit 2 demonstrates that we have also found $p150^{Sal2}$ to be down regulated in a number of human tumors, in addition to ovarian cancer. Ubiquitin normalized cDNA arrays (Clontech), containing matched normal and tumor tissues from cancer patients, were hybridized with a p150 cDNA (*Sal2*) to analyze $p150^{Sal2}$ protein expression. Such arrays included the cDNA from 14 samples of kidney tumors and 11

samples of colon tumors. Out of fourteen kidney tumor samples, ten had a marked down regulation of $p150^{Sal2}$ gene product relative to normal control tissues (about 70% of tumors). Similarly, out of eleven of the colon tumor samples tested, eleven showed a down regulation of $p150^{Sal2}$ (100%). Based on this analysis, a down regulation of the protein is clearly associated with colon and kidney cancers. Techniques to detect protein levels were known in the art at the time of filing of the application and are provided, for example, in the specification on page 20 (lines 11-24).

5. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

2/14/03
Date

Dr. Thomas Benjamin